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| Terms | Documents |
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| wickham-thomas-j$.in. | 13 |

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US Pre-Grant Publication Full-Text Database
JPO Abstracts Database
EPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Refine Search: wickham-thomas-j$.in. Clear

**Search History**

**Today's Date: 9/7/2001**

| DB Name | Query | Hit Count | Set Name |
|---|---|---|---|
| USPT | wickham-thomas-j$.in. | 13 | L1 |

09/612,852

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=> duplicate remove l6
DUPLICATE PREFERENCE IS 'MEDLINE, SCISEARCH, BIOSIS, EMBASE, CAPLUS, WPIDS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L6
L7            10 DUPLICATE REMOVE L6 (17 DUPLICATES REMOVED)

=> display total ibib abs l7

L7   ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2001 ACS         DUPLICATE 1
ACCESSION NUMBER:         2001:31532  CAPLUS
DOCUMENT NUMBER:          134:111234
TITLE:                    Recombinant adenovirus vector with changed
                          tropism due to altered fiber for use
                          in gene therapy
INVENTOR(S):              Lindholm, Leif
PATENT ASSIGNEE(S):       Got-A-Gene, Swed.
SOURCE:                   PCT Int. Appl., 48 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.   DATE
     ---------------   ----  --------      ---------------   --------
     WO 2001002431      A1   20010111      WO 2000-SE1390    20000630
         W:  AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
             CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI,
             GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
             KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,
             MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM,
             TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
             MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                   SE 1999-2601     A  19990706
                                         US 1999-143632   P  19990714
AB   The present invention relates to new recombinant adenovirus with
     changed tropism. In the adenovirus the native
     fiber protein, comprising a fiber tail, a fiber
     shaft and a fiber knob including a trimerization
     motif, has been changed in that the native knob contg. the cell binding
     structure and the native trimerization motif has been removed
     and a new cell-binding ligand and an external trimerization
     motif have been introduced into the virus fiber. The invention
     also relates to the recombinant adenovirus for the treatment of
     human diseases, either in vivo or by in vitro methods. Also included is
a
     method for rescuing of recombinant adenovirus fibers
     into the adenovirus genome.
REFERENCE COUNT:          5
REFERENCE(S):             (1) Genvec Inc; WO 9626281 A1 1996 CAPLUS
                          (2) Genvec Inc; WO 9720051 A2 1997 CAPLUS
                          (3) Susan, C; JOURNAL OF VIROLOGY 1997, V71(6), P4782
                          (4) The Uab Research Foundation; WO 9941359 A1 1999
                              CAPLUS
```

(5) The University Of Alabama At Birmingham Research Foundation; WO 9720575 A1 1997 CAPLUS

L7 ANSWER 2 OF 10 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001200588 MEDLINE
DOCUMENT NUMBER: 21184699 PubMed ID: 11287567
TITLE: Genetic targeting of an adenovirus vector via replacement of the fiber protein with the phage T4 fibritin.
AUTHOR: Krasnykh V; Belousova N; Korokhov N; Mikheeva G; Curiel D T
CORPORATE SOURCE: Division of Human Gene Therapy, Department of Medicine, and the Gene Therapy Center, University of Alabama at Birmingham, Birmingham, Alabama 35294, USA.
CONTRACT NUMBER: N01 CO-97110 (NCI)
R01 CA74242 (NCI)
R01 CA83821 (NCI)
R01 HL50255 (NHLBI)
SOURCE: JOURNAL OF VIROLOGY, (2001 May) 75 (9) 4176-83.
Journal code: KCV; 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010521
Last Updated on STN: 20010521
Entered Medline: 20010517

AB The utility of **adenovirus** (Ad) vectors for gene therapy is restricted by their inability to selectively transduce disease-affected tissues. This limitation may be overcome by the derivation of vectors capable of interacting with receptors specifically expressed in the target tissue. Previous attempts to alter Ad **tropism** by genetic **modification** of the Ad **fiber** have had limited success due to structural conflicts between the **fiber** and the targeting ligand. Here we present a strategy to derive an Ad vector with enhanced targeting potential by a radical replacement of the **fiber protein** in the Ad capsid with a **chimeric** molecule containing a heterologous **trimerization** motif and a receptor-binding ligand. Our approach, which capitalized upon the overall structural similarity between the human Ad type 5 (Ad5) **fiber** and bacteriophage T4 fibritin **proteins**, has resulted in the generation of a genetically **modified** Ad5 incorporating **chimeric fiber**-fibritin **proteins** targeted to artificial receptor molecules. Gene transfer studies employing this novel viral vector have demonstrated its capacity to efficiently deliver a transgene payload to the target cells in a receptor-specific manner.

L7 ANSWER 3 OF 10 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001196602 MEDLINE
DOCUMENT NUMBER: 21126423 PubMed ID: 11222722
TITLE: Adenovirus type 5 viral particles pseudotyped with mutagenized fiber proteins show diminished infectivity of coxsackie B-adenovirus receptor-bearing cells.
AUTHOR: Jakubczak J L; Rollence M L; Stewart D A; Jafari J D; Von Seggern D J; Nemerow G R; Stevenson S C; Hallenbeck P L
CORPORATE SOURCE: Genetic Therapy, Inc./A Novartis Company, Gaithersburg,

Maryland 20878, USA.
SOURCE: JOURNAL OF VIROLOGY, (2001 Mar) 75 (6) 2972-81.
Journal code: KCV; 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010410
Last Updated on STN: 20010410
Entered Medline: 20010405

AB A major limitation of **adenovirus** type 5 (Ad5)-based gene therapy, the inability to target therapeutic genes to selected cell types, is attributable to the natural **tropism** of the virus for the widely expressed coxsackievirus-**adenovirus** receptor (CAR) **protein**. **Modifications** of the Ad5 **fiber** knob domain have been shown to alter the **tropism** of the virus. We have developed a novel system to rapidly evaluate the function of **modified fiber proteins** in their most relevant context, the **adenoviral** capsid. This transient transfection/infection system combines transfection of cells with plasmids that express high levels of the **modified fiber protein** and infection with Ad5.beta gal.Delta F, an E1-, E3-, and **fiber**-deleted **adenoviral** vector encoding beta-galactosidase. We have used this system to test the **adenoviral** transduction efficiency mediated by a panel of **fiber protein** mutants that were proposed to influence CAR interaction. A series of amino acid **modifications** were incorporated via mutagenesis into the **fiber** expression plasmid, and the resulting **fiber proteins** were subsequently incorporated onto **adenoviral** particles. **Mutations** located in the **fiber** knob AB and CD loops demonstrated the greatest reduction in **fiber**-mediated gene transfer in HeLa cells. We also observed effects on transduction efficiency with **mutations** in the FG loop, indicating that the binding site may extend to the adjacent monomer in the **fiber trimer** and in the HI loop. These studies support the concept that **modification** of the **fiber** knob domain to diminish or ablate CAR interaction should result in a detargeted **adenoviral** vector that can be combined simultaneously with novel ligands for the development of a systemically administered, targeted **adenoviral** vector.

L7 ANSWER 4 OF 10 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001332370 MEDLINE
DOCUMENT NUMBER: 21295022 PubMed ID: 11402301
TITLE: Influence of **adenoviral fiber** mutations on viral encapsidation, infectivity and in vivo **tropism**.
AUTHOR: Leissner P; Legrand V; Schlesinger Y; Hadji D A; van Raaij M; Cusack S; Pavirani A; Mehtali M
CORPORATE SOURCE: Transgene SA, Strasbourg, France.
SOURCE: GENE THERAPY, (2001 Jan) 8 (1) 49-57.
Journal code: CCE; 9421525. ISSN: 0969-7128.
PUB. COUNTRY: England: United Kingdom
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010625
Last Updated on STN: 20010625
Entered Medline: 20010621

AB Targeting of adenovirus (Ad)-encoded therapeutic genes to specific cell types has become a major goal in gene therapy. Redirecting the specificity of infection requires the abrogation of the natural interaction between the viral fiber and its cellular receptors (CAR) and the simultaneous introduction of a new binding specificity into the viral capsid. To abrogate the natural affinity of the fiber, we have **mutated** residues presumed to be directly or indirectly involved in CAR-binding in the knob domain of the fiber **protein**. These residues are located in the AB loop (Ser408) and in the DG loop (Tyr491, Ala494, Ala503). The **mutations** Ser408Glu, Tyr491Asp, Ala494Asp and Ala503Asp did not prevent the incorporation of **trimeric** fibers in the viral capsid but led to loss of CAR binding in vitro. Infectivity of the mutant viruses could be restored in vitro by introducing a ligand at the C-terminal end of the knob, confirming that the reduced infectivity of the fiber-**modified** virus was due to an impaired interaction of the viral particle with the CAR receptor. However, after systemic delivery, the in vivo biodistribution of impaired CAR-binding viruses without addition of a specific ligand was not altered when compared with wild-type Ad.

L7 ANSWER 5 OF 10 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2001046608 MEDLINE
DOCUMENT NUMBER: 20523936 PubMed ID: 11070036
TITLE: Recombinant human adenovirus: targeting to the human transferrin receptor improves gene transfer to brain microcapillary endothelium.
AUTHOR: Xia H; Anderson B; Mao Q; Davidson B L
CORPORATE SOURCE: Program in Gene Therapy, Department of Internal Medicine, University of Iowa College of Medicine, Iowa City, Iowa 52242, USA.
CONTRACT NUMBER: DK54759 (NIDDK)
HD33531 (NICHD)
SOURCE: JOURNAL OF VIROLOGY, (2000 Dec) 74 (23) 11359-66.
Journal code: KCV. ISSN: 0022-538X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001204

AB Some inborn errors of metabolism due to deficiencies of soluble lysosomal enzymes cause global neurodegenerative disease. Representative examples include the infantile and late infantile forms of the ceroid lipofuscinoses (CLN1 or CLN2 deficiency, respectively) and mucopolysaccharidoses type VII (MPS VII), a deficiency of beta-glucuronidase. Treatment of the central nervous system component of these disorders will require widespread **protein** or enzyme replacement, either through dissemination of the **protein** or

through dissemination of a gene encoding it. We hypothesize that transduction of brain microcapillary endothelium (BME) with recombinant viral vectors, with secretion of enzyme product basolaterally, could allow for widespread enzyme dissemination. To achieve this, viruses should be **modified** to target the BME. This requires (i) identification of a BME-resident target receptor, (ii) identification of motifs targeted to that molecule, (iii) the construction of **modified** viruses to allow for binding to the target receptor, and (iv) demonstrated transduction of receptor-expressing cells. In proof of principal experiments, we chose the human transferrin receptor (hTfR), a molecule found at high density on human BME. A nonamer phage display library was panned for motifs which could bind hTfR. Forty-three clones were sequenced, most of which contained an AKxxK/R, KxKxPK/R, or KxK motif. Ten peptides representative of the three motifs were cloned into the HI loop of **adenovirus** type 5 **fiber**. All motifs tested retained their ability to **trimerize** and bind transferrin receptor, and seven allowed for recombinant **adenovirus** production. Importantly, the **fiber-modified** viruses facilitated increased gene transfer (2- to 34-fold) to hTfR expressing cell lines and human brain microcapillary endothelia expressing high levels of endogenous receptor. Our data indicate that **adenoviruses** can be **modified** in the HI loop for expanded **tropism** to the hTfR.

L7 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:529241 CAPLUS
DOCUMENT NUMBER: 131:140498
TITLE: **Modified** adenovirus contg. a **chimeric** fiber **protein**, and uses thereof for cancer therapy
INVENTOR(S): Curiel, David T.; Krasnykh, Victor N.
PATENT ASSIGNEE(S): The UAB Research Foundation, USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9941359 | A1 | 19990819 | WO 1999-US3233 | 19990216 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9932940 | A1 | 19990830 | AU 1999-32940 | 19990216 |
| BR 9908018 | A | 20001024 | BR 1999-8018 | 19990216 |
| EP 1070118 | A1 | 20010124 | EP 1999-932506 | 19990216 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, | | | | |

IE, FI

| | | | | | |
|---|---|---|---|---|---|
| US 6210946 | B1 | 20010403 | US 1999-250580 | | 19990216 |
| NO 2000004563 | A | 20000913 | NO 2000-4563 | | 20000913 |
| PRIORITY APPLN. INFO.: | | | US 1998-74844 | P | 19980217 |
| | | | WO 1999-US3233 | W | 19990216 |

AB The present invention provides means to **modify** the **tropism** of recombinant **adenoviral** vectors using genetic methods to alter the **adenoviral fiber** cell-binding **protein** while maintaining the native **trimeric protein** biosynthesis profile. The present invention further provides means to specifically target particular cell types for infection with said recombinant **adenoviral** vectors. In a preferred embodiment, the recombinant **adenovirus** vector comprises **fiber** replacement proteins composed of the **fiber** tail domain, a portion of the fibritin gene from the bacteriophage T4, and a ligand domain. The vector may also encode a therapeutic gene, such as the herpes simplex virus thymidine kinase gene which, along with ganciclovir, can be used to specifically kill tumor cells.

REFERENCE COUNT: 7
REFERENCE(S):
(1) Curiel; US 5871727 A 1999 CAPLUS
(2) McClelland; US 5543328 A 1996 CAPLUS
(3) Spooner; US 5885808 A 1999 CAPLUS
(4) Wickham; US 5559099 A 1996 CAPLUS
(5) Wickham; US 5712136 A 1998 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 10 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-539951 [45] WPIDS
DOC. NO. CPI: C1999-157704
TITLE: Recombinant adenovirus vectors with modified fiber knob loops, useful in gene therapy.
DERWENT CLASS: B04 D16
INVENTOR(S): CURIEL, D T; DMITRIEV, I; KRASNYKH, V N
PATENT ASSIGNEE(S): (UABR-N) UAB RES FOUND
COUNTRY COUNT: 75
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|
| WO 9939734 | A1 | 19990812 | (199945)* | EN | 128 |
| RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW | | | | | |
| W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN | | | | | |
| AU 9926595 | A | 19990823 | (200005) | | |
| NO 2000003956 | A | 20001005 | (200058) | | |
| BR 9908613 | A | 20001031 | (200060) | | |
| EP 1053013 | A1 | 20001122 | (200061) | EN | |
| R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE | | | | | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 9939734 | A1 | WO 1999-US2549 | 19990205 |
| AU 9926595 | A | AU 1999-26595 | 19990205 |

| | | | |
|---|---|---|---|
| NO 2000003956 | A | WO 1999-US2549 | 19990205 |
| | | NO 2000-3956 | 20000804 |
| BR 9908613 | A | BR 1999-8613 | 19990205 |
| | | WO 1999-US2549 | 19990205 |
| EP 1053013 | A1 | EP 1999-906761 | 19990205 |
| | | WO 1999-US2549 | 19990205 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO |
|---|---|---|---|
| AU 9926595 | A | Based on | WO 9939734 |
| BR 9908613 | A | Based on | WO 9939734 |
| EP 1053013 | A1 | Based on | WO 9939734 |

PRIORITY APPLN. INFO: US 1998-99801 19980910; US 1998-73947 19980206

AN 1999-539951 [45] WPIDS

AB WO 9939734 A UPAB: 19991103

NOVELTY - A recombinant **adenovirus** (I) comprising a **fiber** gene modified in the HI loop domain of the **fiber** knob, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) killing tumor cells by:

(a) administering (I), and

(b) treating the individual with ganciclovir;

(2) providing gene therapy by administering (I); and

(3) increasing the ability of an **adenovirus** to transduce a cell by modifying the **fiber** gene in the HI loop domain of the **fiber** knob of (I).

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - None given.

USE - The modified **adenovirus** has an altered **tropism**, which allows the **adenovirus** to be targeted to selected cell types. The recombinant **adenovirus** can be used to provide gene therapy for individuals suffering from cancer, cystic fibrosis and Duchene's muscular dystrophy (claimed).

ADVANTAGE - Incorporation of an RGD containing peptide in the HI loop of the **fiber** knob domain results in the ability of the virus to utilize an alternative receptor during the cell entry process. **Modifying** the **adenovirus fiber** knob **protein** increases the ability of an **adenovirus** to transduce a tumor cell in vitro, in vivo and ex vivo (claimed). The vector Ad5FHIFLAG incorporating an RGD peptide (CDCRGDCFC) demonstrated two to three orders of magnitude of increased gene transfer to ovarian cancer cells.

Dwg.0/27

L7 ANSWER 8 OF 10 MEDLINE DUPLICATE 6

ACCESSION NUMBER: 2000131864 MEDLINE

DOCUMENT NUMBER: 20131864 PubMed ID: 10667212

TITLE: Strategies to adapt adenoviral vectors for targeted delivery.

AUTHOR: Curiel D T

CORPORATE SOURCE: Gene Therapy Center, University of Alabama at Birmingham

35294-3300, USA.. david.curiel@ccc.uab.edu
CONTRACT NUMBER: HL50255 (NHLBI)
RO1CA68245 (NCI)
RO1CA74242 (NCI)
SOURCE: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1999) 886 158-71. Ref: 52
Journal code: 5NM; 7506858. ISSN: 0077-8923.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000229

AB The utility of current generation **adenoviral** vectors for targeted, cell-specific gene delivery is limited by the promiscuous **tropism** of the parent virus. To address this issue, we have developed both genetic and immunologic methods to alter viral **tropism**. Immunologic retargeting has been achieved via conjugates comprised of an antifiber knob Fab and a targeting moiety consisting of a ligand or antireceptor antibody. Gene delivery by this approach has been accomplished via a variety of cellular pathways including receptors for folate, FGF, and EGF. In addition to cell-specific gene delivery, this strategy has allowed enhanced gene delivery to target cells lacking the native **adenoviral** receptor, CAR. Of note, this specific and extended gene delivery allowed enhanced survival in murine models of human carcinoma via cancer gene therapy. Genetic strategies to alter **adenoviral tropism** have included both **fiber modification** and **fiber** replacement. In the former, we have identified the HI loop of **fiber** as a propitious locale for introduction of heterologous peptides. Incorporation of an RGDC peptide at this locale allowed gene delivery via cellular integrins with dramatic efficiency augmentations. As a strategy to achieve both new **tropism** as well as to ablate native **tropism**, methods have been developed to replace the **fiber protein** with heterologous motif which preserves the key **trimeric** quaternary structure of **fiber** and allows for propagation. Such a **fiber**-replacement virus has been rescued and has demonstrated capacities consistent with its utility as a novel vector agent. These strategies have allowed the achievement of cell-specific gene delivery via **adenoviral** vectors and thus have the potential to enhance the utility of this vector agent.

L7 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:640334 CAPLUS
DOCUMENT NUMBER: 129:255990
TITLE: **Adenoviral** vectors with **chimeric fiber proteins** for altered cell **tropism** as well as vector purification
INVENTOR(S): Curiel, David T.; Krasnykh, Victor; Dimitriev, Igor
PATENT ASSIGNEE(S): UAB Research Foundation, USA
SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9841618 | A1 | 19980924 | WO 1998-US3879 | 19980313 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9864429 | A1 | 19981012 | AU 1998-64429 | 19980313 |

PRIORITY APPLN. INFO.: US 1997-40703 19970314
US 1997-54112 19970729
WO 1998-US3879 19980313

AB The utility of current recombinant adenovirus vectors for gene therapy applications is improved by designing targeted vectors capable of gene delivery to selected cell types in vivo. In order to achieve such targeting, incorporation of ligands in the adenoviral fiber protein, in which the protein mediates primary binding of adenovirus to its cell surface receptor, utilizes the HI loop of the fiber knob as a convenient locale for incorporation of heterologous ligands. Recombinant fiber proteins expressed in a variety of cells including baculovirus-infected insect cells and E. coli to demonstrate that the incorporation of the FLAG octapeptide into the HI loop does not ablate fiber **trimerization** and does not disturb formation of the cell-binding site localized in the knob. A recombinant adenovirus of the instant invention having this modified fiber shows that a short peptide sequence engineered in the knob is compatible with the biol. functions of the fiber. A peptide incorporated into the knob according to the invention remains available for binding in the context of mature virions contg. modified fibers. The invention incorporates heterologous ligands into the HI loop of the fiber knob and the properties of this locale are consistent with its employment in adenovirus re-targeting strategies.

L7 ANSWER 10 OF 10 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-059848 [05] WPIDS
DOC. NO. CPI: C1999-017684
TITLE: New adenoviral fibre **trimer** with reduced binding to native substrate - useful for, e.g. preparing gene therapy vector with minimal ectopic infection for in vitro applications.
DERWENT CLASS: B04 D16
INVENTOR(S): BROUGH, D E; EINFELD, D; KOVESDI, I; LIZONOVA, A; ROELVINK, P W; WICKHAM, T J; YONEHIRO, G
PATENT ASSIGNEE(S): (GENV-N) GENVEC INC
COUNTRY COUNT: 83
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---|---|---|---|---|---|

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WO 9854346 A1 19981203 (199905)* EN 108
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9876049 A 19981230 (199918)
EP 988390 A1 20000329 (200020) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
CZ 9904223 A3 20000517 (200031)
SK 9901599 A3 20000612 (200036)
BR 9809173 A 20000801 (200043)
HU 2000002070 A2 20001030 (200064)

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| WO 9854346 | A1 | WO 1998-US11024 | 19980528 |
| AU 9876049 | A | AU 1998-76049 | 19980528 |
| EP 988390 | A1 | EP 1998-923856 | 19980528 |
| | | WO 1998-US11024 | 19980528 |
| CZ 9904223 | A3 | WO 1998-US11024 | 19980528 |
| | | CZ 1999-4223 | 19980528 |
| SK 9901599 | A3 | WO 1998-US11024 | 19980528 |
| | | SK 1999-1599 | 19980528 |
| BR 9809173 | A | BR 1998-9173 | 19980528 |
| | | WO 1998-US11024 | 19980528 |
| HU 2000002070 | A2 | WO 1998-US11024 | 19980528 |
| | | HU 2000-2070 | 19980528 |

FILING DETAILS:

| PATENT NO | KIND | | PATENT NO |
|---|---|---|---|
| AU 9876049 | A | Based on | WO 9854346 |
| EP 988390 | A1 | Based on | WO 9854346 |
| CZ 9904223 | A3 | Based on | WO 9854346 |
| BR 9809173 | A | Based on | WO 9854346 |
| HU 2000002070 | A2 | Based on | WO 9854346 |

PRIORITY APPLN. INFO: US 1998-71668 19980116; US 1997-47849 19970528

AN 1999-059848 [05] WPIDS

AB WO 9854346 A UPAB: 19990203

New primer (I) consists of monomers (II) each having: (i) an N-terminus of an **adenoviral fibre protein** (A), and (ii) a **trimerisation** domain (TD) is new. (I) has lower affinity for native substrate than the native **adenoviral fibre trimer**. Also new are: (1) composition (B) of (I) plus an **adenoviral** penton base (III); (2) **adenovirus** containing (I); (3) cell line (C) expressing a non-natural cell-surface receptor to which **adenovirus** having an appropriate ligand can bind; (4) methods for purifying or inactivating **adenovirus** having a substrate-specific ligand, and (5) **chimaeric** blocking

**protein** (IV) that includes a substrate for **adenoviral fibre**.

USE - The cell lines of (3) are used: (i) to propagate **adenovirus** for use as gene therapy vectors (for in vitro or in vivo applications); (ii) as reagents for studying **adenoviral** attachment and infection, and (iii) in receptor-ligand interaction assays.

(I) can be used in similar assays and as adhesion proteins. Method (4) is particularly used to inactivate **adenovirus** in blood or lymph and (IV) are used to interfere with **adenoviral** targeting, i.e. to reduce native **tropism** and alter **adenoviral** receptor binding.

ADVANTAGE - The new viruses produce minimal ectopic infection (they can not infect native host cells) so are safer as vectors and can be engineered for selective targeting to other cells.

Dwg.0/17

=>

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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Dec 17   The CA Lexicon available in the CAPLUS and CA files
 NEWS  3  Feb 06   Engineering Information Encompass files have new names
 NEWS  4  Feb 16   TOXLINE no longer being updated
 NEWS  5  Apr 23   Search Derwent WPINDEX by chemical structure
 NEWS  6  Apr 23   PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
 NEWS  7  May 07   DGENE Reload
 NEWS  8  Jun 20   Published patent applications (A1) are now in USPATFULL
 NEWS  9  JUL 13   New SDI alert frequency now available in Derwent's
                   DWPI and DPCI
 NEWS 10  Aug 23   In-process records and more frequent updates now in
                   MEDLINE
 NEWS 11  Aug 23   PAGE IMAGES FOR 1947-1966 RECORDS IN CAPLUS AND CA
 NEWS 12  Aug 23   Adis Newsletters (ADISNEWS) now available on STN

 NEWS EXPRESS  August 15 CURRENT WINDOWS VERSION IS V6.0c,
               CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP),
               AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001
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=> s trimeriz?(w)chimer?(w)prot?
   3 FILES SEARCHED...
   5 FILES SEARCHED...
L1             0 TRIMERIZ?(W) CHIMER?(W) PROT?

=> s adenovir?(p)tropism(p)(fiber or fibre)
L2           263 ADENOVIR?(P) TROPISM(P)(FIBER OR FIBRE)

=> s l1 and trimeri?
L3             0 L1 AND TRIMERI?

=> s l1 and trime?
L4             0 L1 AND TRIME?

=> s l2 and trimer?
L5            39 L2 AND TRIMER?

=> s l5 and (chim? or modif? or mutat?) (s)prot?
   3 FILES SEARCHED...
   5 FILES SEARCHED...
L6            27 L5 AND (CHIM? OR MODIF? OR MUTAT?) (S) PROT?

=> display total ibib abs l6
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